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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,159	NYBERG ET AL.	
	Examiner	Art Unit	
	DANIEL KOLKER	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-9,13-22,24-26 and 30-65* is/are pending in the application.

4a) Of the above claim(s) *14-21 and 31-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,13,22,24-26,30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The remarks and amendments filed 21 December 2007 have been entered. Claims 4, 10 – 12, 23, and 27 – 29 are canceled. Claims 1 – 3, 5 – 9, 13 – 22, 24 – 26, and 30 – 65 are pending.

Election/Restrictions

2. Claims 14 – 21 and 31 – 65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 18 April 2007.

Claims 1 – 3, 5 – 9, 13, 22, 24 – 26, and 30 are under examination.

Withdrawn Rejections and Objections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. Any objection or rejection of a claim now canceled is moot.

B. The objection to claim 22 is withdrawn in light of the amendments which correct the awkward language.

C. The rejection of claim 6 under 35 USC 112, second paragraph, is withdrawn in light of the amendments which clarify the scope of the claim.

Rejections and Objections Necessitated by Amendment

Claim Objections

4. Claims 24 – 26 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The claims allow for administration of proteins with activities related to SEQ ID NO:4 (claims 24 - 25) or administration of SEQ ID NO:4 itself (claim 26). However the claims depend from claim 22, which does not recite SEQ ID NO:4 but rather is limited to SEQ ID NO:2 and certain variants. As claims 24 – 26 broaden rather than narrow the scope of patent protection sought, they are objected to.

Double Patenting

5. Applicant is advised that should claim 9 be found allowable, claim 13 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 9 and 13 are of identical scope; both depend directly from claim 1 and require administration of a compound which "is identical to SEQ ID NO:2" (claim 9) or "is SEQ ID NO:2" (claim 13).

Maintained Rejections and Objections

Priority

6. The effective filing date of claims 1 – 3, 5 – 9, and 13 is 11 June 2002 for the reasons previously made of record. Applicant stated, on p. 11 of the remarks filed 21 December 2007, that all references to SEQ ID NO:4 have been removed, implying that all claims should receive benefit of 11 June 2002 as their effective filing date. Due to applicant's amendments, claims 22 and 30 are entitled to 11 June 2002 as the appropriate effective filing date. However, it is noted that claims 24 – 26 still encompasses administration of SEQ ID NO:4 or compounds with activity of SEQ ID NO:4. Therefore the effective filing date of claims 24 – 26 is 11 June 2003, the date that PCT/EP03/06207 was filed. Applicant did not traverse the examiner's determination that this date is the first disclosure of instant SEQ ID NO:4.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 3, 5 – 9, 13, 22, and 24 - 25 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for administration of compounds at least 95% identical to SEQ ID NO:2 wherein the compound increases proliferation of hippocampal progenitor cells, does not reasonably provide enablement for administration of proteins at least 80% - 99% identical to SEQ ID NO:2 as broadly claimed, or for administration of proteins with any "activity" as recited in claims 7 – 8 and 24 – 25, or for ameliorating all

conditions caused or characterized by abnormal cell loss as recited in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection is maintained for the reasons previously made of record and explained in further detail herein. The claims remain considerably broader than what is enabled by the specification for several reasons:

1) The claims encompass administration of compounds at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to SEQ ID NO:2 (see for example independent claims 1 and 22). No particular structural regions must be preserved in the compounds to be administered. No particular functional activity of the compounds is recited in the claims. The skilled artisan could not make the full scope of products required in the absence of undue experimentation, given what is encompassed by these broad claims and what is disclosed by the comparatively more narrow specification.

The specification discloses that porcine GIP, which differs from SEQ ID NO:2 by three amino acids, attenuates weight gain (see p. 33 and Figure 5). Given that SEQ ID NO:2 is 42 amino acids long, three amino acid changes represents about a 7% variation from the disclosed sequence. The specification therefore provides adequate guidance for inhibiting obesity by administering a protein at least 95% identical to SEQ ID NO:2 wherein the protein attenuates weight gain in an animal. However, claim 22 encompasses administration of proteins that are only 80% identical to SEQ ID NO:2 which need not have any particular activity preserved. Claims 7 – 8 and 24 – 25 allow for any "activity" to be present but no particular activity, such as the ability to increase cell proliferation or reduce body weight, is recited in the claims. The specification fails to provide sufficient working examples commensurate in scope with the breadth of the claims, and fails to provide adequate guidance as to what activities should be preserved. Given that the claims allow for up to 20% of the protein sequence to be deleted or changed, and allow for insertions anywhere within the sequence until the 80% sequence threshold is reached, the skilled artisan would have to undertake a great deal of experimentation just to make the full scope of possible variants to be administered in the claimed methods. Even after the variants were made, the artisan would have to determine which "activities" are required for success in the claimed methods, and then would have to determine which structural elements in the variants are necessary and sufficient for these functions. As Alberts (previously made of record) teaches that the function of a protein is dependent upon its structure, the

artisan would need to make the structure-function correlations for the variants and all possible activities thereof in order to know which products to use for which conditions. Given the paucity of working examples and the lack of guidance commensurate with the full breadth of the claims, the large degree of experimentation required would be undue. Additionally, the skilled artisan would have to determine how to increase the appropriate activities of the variants in order to practice the methods of claims 8 and 25. In order to do this, the artisan would have to arrive at an understanding of which structures should be added to the protein to increase its activity. Again, there is not sufficient guidance in the specification or the art of record as to how to accomplish this. The remaining claims are rejected as they depend from a rejected base or intermediate claim but are not limited to subject matter which could be accomplished in the absence of undue experimentation.

2) Claims 1 – 3, 5 – 9, and 13 encompass amelioration of symptoms of any and all diseases or conditions either caused or characterized by abnormal cell loss. Certain specific conditions are recited in claim 6. The specification show increase of proliferation of hippocampal progenitors following administration of porcine GIP, but shows no amelioration of symptoms of any disease or condition. The skilled artisan would immediately realize that since porcine GIP (a protein more than 90% identical to SEQ ID NO:2) *increases* proliferation of cells, it would not be effective in those conditions caused or characterized by excessive proliferation such as brain cancer. As excessive proliferation is "abnormal loss of cells" as recited in claim 1 (excess proliferation is often the result of inadequate cell death), proliferation-promoting compounds such as SEQ ID NO:2 or variants which increase proliferation of cells thereof would not be expected to be effective in these conditions. Additionally, as set forth on p. 8 first complete paragraph of the office action mailed 22 June 2007, the art recognized that increasing brain progenitor cell proliferation is not a reasonable animal model for any particular disease, and results in such experiments are not predictive of therapeutic efficacy. Thus the claims are not enabled for inhibiting and/or relieving conditions caused or characterized by abnormal cell loss as recited in claim 1.

8. Claims 1 – 3, 5 – 8, 22, and 24 – 25 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Independent claims 1 and 22 each allow for administration of products which vary by up to 20% from SEQ ID NO:2. There is no requirement that any particular region be conserved, and there is no requirement that any particular functional activity be present. Dependent claims 7 – 8 and 24 – 25 are drawn to administration of variants that have either more or less "activity" than SEQ ID NO:2. The specification fails to disclose to the skilled artisan which structures should be maintained, changed, inserted, or deleted such that the "activity" of the protein is increased or decreased as required by the claims. While the specification discloses administration of porcine GIP, which is over 90% identical to SEQ ID NO:2, the skilled artisan cannot envision the full genus of products to be administered which includes those only 80% identical to same, and cannot envision the structures common to all members of this genus. Additionally, the skilled artisan cannot envision the structures that impart decreased activity to the variants as recited in claims 7 and 24, or the structures that impart increased activity to the variants as recited in claims 8 and 25. Accordingly, the invention of claims 1, 7 – 8, 22, and 24 - 25 has not been fully described. Claims 2 - 3 and 5 - 6 are rejected as they depend from rejected claim 1, but are not limited to subject matter which is fully described by the specification.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 – 3, 5 – 9, 13, 22, 24 – 26, and 30 stand rejected under 35 U.S.C. 102(b) as being anticpated by Bollag (2001. Molecular and Cellular Endocrinology 177:35 – 41, cited on IDS filed 25 January 2006).

This rejection stands for the reasons previously made of record and explained in further detail below. Briefly, Bollag teaches methods of administering human GIP to animal subjects. The specification discloses that human GIP has the sequence of SEQ ID NO:2 (see p. 2 final

paragraph). Applicant did not traverse the examiner's determination that the product administered by Bollag is the same as instant SEQ ID NO:2, encompassed by claims 1, 7 – 9, 13, 22, 24 - 26, and 30. Bollag teaches that animals that received GIP (i.e., SEQ ID NO:2) gained weight no faster than those who received a control injection (p. 39 second column). Administration of the product is sufficient to inhibit obesity, as animals who receive it are not obese. Therefore, the reference anticipates claims 22, 26, and 30, drawn to inhibiting obesity by administering SEQ ID NO:2. Note that claim 22 does not require that the subject be obese; rather it encompasses inhibiting obesity in subjects in need of inhibition; as obesity is unhealthy, even normal-weight subjects are in need of inhibition of obesity. Claims 24 – 25 are also anticipated as SEQ ID NO:2 has activity at least about 99% of its own activity, as recited in claim 24, and has "an activity that corresponds to at least about 100%" of its own activity, as recited in claim 25.

Claim 1 is anticipated as the administration of SEQ ID NO:2 will inherently inhibit conditions caused or characterized by abnormal loss of cells. Note that this claim does not require that the subject have any such condition; rather it encompasses prophylactic administration to asymptomatic subjects. The claim encompasses inhibiting conditions in subjects in need of inhibition; all healthy subjects are in need of inhibition of developing disease. Claims 2 – 3 and 5 recite certain types of abnormal cell loss. However since the claims encompass inhibiting disease and allow for administration of the compound to asymptomatic persons, the reference by Bollag anticipates these claims. Similarly, claim 6 does not require that the patient have any of these condition, but is construed as inhibiting development of such conditions. The claim does not require any steps beyond administering a compound at least about 80% identical to SEQ ID NO:2, which is taught by Bollag. Claims 7 - 8 are also anticipated as SEQ ID NO:2 has activity at least about 99% of its own activity, as recited in claim 7, and has "an activity that corresponds to at least about 100%" of its own activity, as recited in claim 8. Claims 9 and 13 are anticipated as the compound is identical to SEQ ID NO:2.

Applicant argues, on p. 16 of the remarks, that the Bollag reference does not anticipate the claimed invention. Specifically, applicant argues that amending the claims to require administration to subjects "in need" of inhibiting or relieving the conditions is sufficient to overcome the rejection. The examiner disagrees. As set forth above, all patients are in need of inhibiting the development of diseases and conditions such as brain cancer, encompassed by

claim 1, and Alzheimer's disease, recited in claim 6. All subjects are in need of inhibiting obesity, even those who are not obese. Independent claims 1 and 22 do not require any steps other than administration of the relevant compounds. They do not require selecting patients, and are not limited to patients who have or are suffering from any particular diseases or conditions. Therefore, the rejection is maintained.

Conclusion

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL KOLKER whose telephone number is (571)272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D.K./
Patent Examiner, Art Unit 1649
March 7, 2008

/Robert C. Hayes, Ph.D./
Primary Examiner, Art Unit 1649